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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,532	07/16/2003	Peggy J. Farnham	960296.98750	3318
26734	7590	01/06/2006	EXAMINER	
QUARLES & BRADY LLP FIRSTAR PLAZA, ONE SOUTH PINCKNEY STREET P.O. BOX 2113 SUITE 600 MADISON, WI 53701-2113			AEDER, SEAN E	
		ART UNIT		PAPER NUMBER
				1642

DATE MAILED: 01/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/620,532	FARNHAM ET AL.	
	Examiner Sean E. Aeder, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 21 November 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 11-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 11-16 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 7/16/03 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input checked="" type="checkbox"/> Other: <u>sequence comparison</u> . |

Detailed Action

The Election filed 11/21/05 in response to the Office Action of 9/23/05 has been acknowledged and has been entered. Applicant elected group II and SEQ ID NO:4 with traverse.

The traversal is on the ground(s) that a search and examination of all of the inventions would not impose a serious burden on the examiner. Applicants argue that groups I-IX are directed at highly related subject matter and thus can be examined together without serious burden. Applicants further state that "According to MPEP 803.04, ten independent and distinct nucleotide sequences will be examined in a single application without restriction. Applicants believe that the same applies to amino acid sequences." Thus, Applicants request that SEQ ID NO:2 and SEQ ID NO:4 be examined together. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Office Action. The method groups outlined in the restriction includes distinct methods of screening and distinct methods of diagnosis. Each of these methods is further unrelated, as they comprise distinct steps and utilize different products, which demonstrates that each method has a different mode of operation. Searching and examining each of these methods would result in a serious burden on the examiner. Furthermore, the product groups outlined in the restriction requirement includes distinct nucleic acids, distinct polypeptides, and distinct antibodies. Searching and examining

Art Unit: 1642

each of these products would result in a serious burden on the examiner. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. Furthermore, MPEP 803.04 does not state that ten independent and distinct nucleotide sequences are required to be examined in a single application without restriction. MEPE 803.04 states that polynucleotide molecules defined by their nucleic acid sequences constitute independent and distinct inventions and the examiner is permitted to allow a reasonable number of sequences in a single application, which the MPEP suggests may be ten sequences. However, since this rule was written, the size of the sequence databases has grown exponentially. Currently, there are approximately eight different databases that accompany the results of a search of one discrete amino acid or nucleotide sequence and each result set from a particular database must be carefully considered. Hence, the search of multiple different polypeptides, and different polypeptide segments in the databases would require an unreasonable amount of searching and review. Therefore, the Office is currently restricting applications to one independent and distinct nucleotide sequence. For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-39 are pending.

Claims 1-10 and 17-39 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 11-16 are currently under consideration.

Specification

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (paragraphs 27, 50, and 51). Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable codes. See MPEP § 608.01.

Drawings

The drawings are objected to because the poor resolution of Figures 3 and Figures 4 make it impossible to interpret the data. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If

the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 11-16 are objected to for being dependent upon withdrawn claims.
Appropriate correction is required.

Claims 11-16 are objected to for being drawn to non-elected subject matter.
Appropriate correction is required.

For examination purposes: Claim 11 is drawn to an isolated polypeptide comprising amino acids 22-400 of SEQ ID NO:4 or an isolated polypeptide comprising a sequence that is at least 68% identical to amino acids 22-400 of SEQ ID NO:4, claim 12 is drawn to an isolated polypeptide consisting of a sequence encoded by amino acids 22-400 of SEQ ID NO:4 or an isolated polypeptide consisting of a sequence that is at least 68% identical to amino acids 22-400 of SEQ ID NO:4, claim 13 is drawn to an isolated polypeptide comprising amino acids 22 to amino acid 400 of SEQ ID NO:4, claim 14 is drawn to an isolated polypeptide comprising SEQ ID NO:4 or an isolated polypeptide comprising a sequence 70% identical to SEQ ID NO:4, claim 15 is drawn to an isolated polypeptide consisting of SEQ ID NO:4 or an isolated polypeptide consisting

of a sequence 70% identical to SEQ ID NO:4, and claim 16 is drawn to an isolated polypeptide comprising SEQ ID NO:4.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claims are broadly drawn to polypeptides with homology to amino acid sequence SEQ ID NO:4. However, neither the specification nor any art of record teaches how the polypeptide functions or a specific and well-established utility for any of the polypeptides claimed. Furthermore, while it is noted that the specification appears to teach a potential utility for a nucleic acid that encodes amino acids corresponding to SEQ ID NO:4 (see Figures 3 and 4, in particular), the specification fails to provide a nexus between the claimed polypeptides and any specific pathology or establish any involvement in the etiology of any specific disease.

Further, those of skill in the art recognize that overexpression of a particular nucleic acid specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. Thus, it would require further exploration and experimentation in order to assess any predictable utility SEQ ID NO4. For

example, there are many steps in the pathway leading from DNA to protein, and all of them can, in principle, be regulated. For example, Alberts *et al.* (*Molecular Biology of the Cell*, 3rd edition, 1994, page 465) illustrate post-transcriptional regulation of ferritin wherein the translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferin receptor polypeptide is translated. Lewin, B. also teaches (*Genes VI*, Oxford University Press, Inc., NY, Chapter 29, 1997) that a major control point for genes exists during the initiation of transcription by the interaction of the RNA polymerase with its promoter. Concurring with Alberts *et al.*, Lewin further acknowledges downstream control of gene expression since translation of mRNA in the cytoplasm is also a point of control. Also, with regards to tumor associated antigens, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Furthermore, Mallampalli *et al.* (*Biochem. J.* Vol. 318, 1996, pages 333-341) teach that the glucocorticoid, betamethasone, increased mRNA expression of cholinephosphate cytidylyltransferase (CT) as determined by RT-PCR and Southern analysis, but did not *alter* the levels of the polypeptide, i.e. the CT enzyme as assayed by Western blotting (abstract, and page 339, 2nd column, 2nd paragraph). Further, Lewin acknowledges that control of gene expression can occur at multiple stages and that production of RNA *cannot inevitably* be equated with production of protein. Thus, the predictability of protein translation and its possible utility as a diagnostic are not

necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Finally, Greenbaum *et al.* (Genome Biology, 2003, Vol. 4, Issue 9, pages 117.1-117.8) cautions against assuming that mRNA levels are generally correlative of protein levels. The reference teaches (page 117.3, 2nd column) that primarily because of a limited ability to measure protein abundances, researchers have tried to find correlations between mRNA and the limited protein expression data, in the hope that they could determine protein abundance levels from the more copious and technically easier mRNA experiments. To date, however, there have been only a handful of efforts to find correlations between mRNA and protein expression levels, most notably in human cancers and yeast cells. And, for the most part, they have reported only minimal and/or limited correlations. The reference further teaches (page 117.4, 2nd column) that there are presumably at least three reasons for the poor correlations generally reported in the literature between the level of mRNA and the level of protein, and these may not be mutually exclusive. First, there are many complicated and varied post-transcriptional mechanisms involved in turning mRNA into protein that are not yet sufficiently well defined to be able to compute protein concentrations from mRNA; second, proteins may differ substantially in their *in vivo* half lives; and/or third, there is a significant amount of error and noise in both protein and mRNA experiments that limit our ability to get a clear picture. The reference further notes (page 117.6, page 2nd column) that to be fully able to understand the relationship between mRNA and protein abundances, the dynamic processes involved in protein synthesis and degradation have to be better understood. Thus, in the absence of any

correlation between the claimed polypeptide(s) with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for antibodies directed to the disclosed polypeptides. Thus, because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-16 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know *how to use* the claimed invention.

Claims 11, 12, 14, and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:4 and therefore the written

description is not commensurate in scope with the claims which read on allelic variants of SEQ ID NO: 4.

The claims are drawn to polypeptides having at least 68% or 70% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. Further, there is no identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed.*” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF’s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from

its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11, 12, 14, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Paturajan et al (US2004/0029790 A1, filed 7/2/02).

Claims 11, 12, 14, and 15 are drawn to sequences with greater than 68% identity to instant SEQ ID NO:4.

Paturajan et al teaches a 416 amino acid sequence that shares 85% identity with instant SEQ ID NO:4 (see comparison of SEQ ID NO:42 with instant SEQ ID NO:4).

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA



**GARY B. NICKOL, PH.D.
PRIMARY EXAMINER**

QY 361 TSQSYLMLAYNMEDQHLYSWEDQHMLYYPVQFPLSTTINQ 400
Ddb 361 TSQSYLMLAYNMEDQHLYSWEDQHMLYYPVQFPLSTTINQ 400

RESULT 2 US-10-467-102 Application US/10467102
; Sequence 3 Application US/10467102
; Publicat on No US20050074762A1
; GENERAL INFORMATION:
; APPLICANT: Yamamoto, Yusuke
; APPLICANT: Sugano, Sumio
; APPLICANT: Isono, Takashi
; APPLICANT: Kawabe, Hiroyuki
; TITLE OF INVENTION: diponeceton-Associated Protein
; FILE REFERENCE: 03/142
; CURRENT APPLICATION NUMBER: US/10/467,102
; FILING DATE: 2003-08-01
; PRIORITY NUMBER: PCT/JP02/00844
; PRIORITY NUMBER: PCT/JP02/00844
; PRIORITY NUMBER: JP 2001-25962
; PRIORITY NUMBER: JP 2001-25962
; NUMBER OF SEQ ID NOS: 3
; SOFTWARE: PatentIn Version 3.1
; SEQ ID NO: 3
; LENGTH: 551
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-467-102-3

Query Match	Match Score	Length	DB
Best Local Similarity	91.1%	DB 5;	
Matches 383; Conservative	86.8%	DB 145;	
Matches 11;	6; Mismatches	Indels 41;	G
1	MLMMMTYSMVPYRVMVLDLNSTKCTLT	-----	-GPGAGGLPGHNGLGDQGPQGCG
1.1	MLMMMTYSMVPYRVMVLDLNSTV	-----	-----
5.5	KGANGKRGKGKGIPGAAGNPGERGE	-----	GPROPSMFNQCPGETCAIPNDDTLVG
17.1	KGANGKRGKGKGIPGAAGNPGERG	-----	-----
11.4	AKGDQGPQGPQGPQGPQGPQGPQGP	-----	-----
23.1	AKGDQGPQGPQGPQGPQGPQGPQGP	-----	-----
17.4	K-----AKSMITSIGIHPYQVKVTFEN	-----	TIRE SANKSDDRIWTHFRPSG - -
2.91	KASEHHHSPOAESMATSCHPQVQLKVTF	-----	TIRE SANKSDDRIWTHFRPSGIMV
21.9	-PPSIL-----FPMIWARC-----LQQISLLPQRG-----	-----	----- PBFQGTSQSITURL
35.1	DQFSILNGSYPTFHIIPIYYPHGGCHRVVYNNNSLYTHKGSITLVRREFQETSQITKL	-----	-----
26.0	YFDKRYLFANSCTYFNLADEBKGWIIYASSVGDSSIIYVQHLBERTPSVYQHYNTT	-----	-----
4.11	YFDKRYLFANSCTYFNLADEBKGWIIYASSVGDSSIIYVQHLBERTPSVYQHYNTT	-----	-----
32.0	KAGNAIAGSILYTDIKMRVTPAPDLGGKQINANFDRSISVYMLAYINNRD	-----	-----
4.71	KAGNAIAGSILYTDIKMRVTPAPDLGGKQINANFDRSISVYMLAYINNRD	-----	-----
38.0	SWIGHALMYPQFLSTTLNQ 400	-----	-----
53.1	SWIGHALMYPQFLSTTLNQ 551	-----	-----

